## **EAST Search History**

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	3251	"calcium citrate"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:44
L2	13165	HDL	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:44
L3	1841	"high-density lipoprotein"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:44
L4	13606	L2 or L3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:45
L5	74	L1 and L4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:49
L6	4278	postmenopausal	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:49
L7	74	L5 and L4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 12:50
L8	24	L5 and L6	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 13:49
L9	74	L1 and L4	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON .	2006/03/21 14:13

## **EAST Search History**

L10	1190	"estrogen replacement therapy"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 14:14
L11	9	L7 and L10	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 14:18
L12	24	L6 and L9	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2006/03/21 14:18

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LOGINID: SSSPTA1617SXK

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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FILE 'HOME' ENTERED AT 14:32:00 ON 21 MAR 2006

=> file reg COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

FILE 'REGISTRY' ENTERED AT 14:32:42 ON 21 MAR 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8 DICTIONARY FILE UPDATES: 20 MAR 2006 HIGHEST RN 877371-73-8

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TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

=> s calcium citrate 88956 CALCIUM 5902 CITRATE 75 CITRATES

5902 CITRATE (CITRATES)

L1 6 CALCIUM CITRATE (CALCIUM(W)CITRATE)

=> s calcium citrate/cn

L2 1 CALCIUM CITRATE/CN

=> d str cn rn

L2 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN

$$\begin{array}{c} \text{CO}_2\text{H} \\ | \\ \text{HO}_2\text{C} - \text{CH}_2 - \text{C} - \text{CH}_2 - \text{CO}_2\text{H} \\ | \\ \text{OH} \end{array}$$

●x Ca

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

CN 1,2,3-Propanetricarboxylic acid, 2-hydroxy-, calcium salt (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Calcium citrate (6CI)

CN Citric acid, calcium salt (8CI)

OTHER NAMES:

CN Citramar

CN E 333

RN 7693-13-2 REGISTRY

=> file caplus medline biosis embase

COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 17.06 17.27

FULL ESTIMATED COST

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FILE 'EMBASE' ENTERED AT 14:33:46 ON 21 MAR 2006 Copyright (c) 2006 Elsevier B.V. All rights reserved.

=> s 7693-13-2/rn

'RN' IS NOT A VALID FIELD CODE

'RN' IS NOT A VALID FIELD CODE

'RN' IS NOT A VALID FIELD CODE

L3 1162 7693-13-2/RN

=> s calcium citrate

L4 2063 CALCIUM CITRATE

=> s calcium and citrate

L5 17375 CALCIUM AND CITRATE

=> s L4 or L5

L6 17375 L4 OR L5

=> s L3 or L6

L7 17512 L3 OR L6

=> s HDL or hight density lipoprotein

L8 112539 HDL OR HIGHT DENSITY LIPOPROTEIN

```
=> s HDL or high density lipoprotein
         150985 HDL OR HIGH DENSITY LIPOPROTEIN
=> s high density lipoprotein
        102670 HIGH DENSITY LIPOPROTEIN
=> s L7 and L8
     17 L7 AND L8
L11
=> dup rem L11
PROCESSING COMPLETED FOR L11
              11 DUP REM L11 (6 DUPLICATES REMOVED)
=> s postmenopausal
         82255 POSTMENOPAUSAL
L13
=> s L12 and L13
L14
              3 L12 AND L13
=> d 1-3 ibib abs
L14 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:696671 CAPLUS
DOCUMENT NUMBER:
                            137:216323
                           Method of administering calcium
TITLE:
                            citrate
INVENTOR(S):
                           Reid, Ian R.
                        Uniservices Ltd., N. Z.
U.S. Pat. Appl. Publ., 13 pp.
PATENT ASSIGNEE(S):
SOURCE:
                            CODEN: USXXCO
DOCUMENT TYPE:
                            Patent
LANGUAGE:
                            English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
                      KIND DATE APPLICATION NO. DATE
      PATENT NO.
     US 2002128320 A1 20020912 US 2001-16371 20011210
WO 2003049668 A2 20030619 WO 2002-IB5759 20021210
WO 2003049668 A3 20040617
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, TC, TT, TT, TT, MA, MD, MG, MK, MN, MW, MZ, NO, NZ, OM, PH.
              LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
               PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
               UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
               KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
               FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ,
               CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                                  US 2001-16371 A 20011210
PRIORITY APPLN. INFO.:
     A method of increasing a high-d. lipoprotein level in plasma of a
     postmenopausal woman by administering a pharmaceutical formulation
      containing calcium citrate is described. The
      therapeutically ED of calcium citrate is equivalent to at
      least about 1 g elemental calcium. An oral pharmaceutical
      composition and a dietary supplement comprises calcium
      citrate in an amount sufficient to provide about 10 mg to about 1 g
      elemental calcium to a diet of a postmenopausal woman.
L14 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN
                      2002:211581 CAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                            136:385392
TITLE:
                            Effects of calcium supplementation on serum
```

lipid concentrations in normal older women: A

randomized controlled trial

Reid, Ian R.; Mason, Barbara; Horne, Anne; Ames, Ruth; AUTHOR(S):

Clearwater, Judith; Bava, Usha; Orr-Walker, Brandon;

Wu, Fiona; Evans, Margaret C.; Gamble, Gregory D.

CORPORATE SOURCE: Department of Medicine, University of Auckland,

Auckland, N. Z.

SOURCE: American Journal of Medicine (2002), 112(5), 343-347

CODEN: AJMEAZ; ISSN: 0002-9343

Excerpta Medica, Inc. PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

To determine the effect of supplementation with Ca citrate on circulating lipid concns. in normal older women. As part of a study of the effects of Ca supplementation on fractures, the authors randomly assigned 223 postmenopausal women (mean [± SD] age, 72 ± 4 yr), who were not receiving therapy for hyperlipidemia or osteoporosis, to receive Ca (1 g/d, n = 111) or placebo (n = 112) for 1 yr. Fasting serum lipid concns., including high-d. lipoprotein (HDL) cholesterol and low-d. lipoprotein (LDL) cholesterol, were obtained at baseline, and at 2, 6, and 12 mo. After 12 mo, HDL cholesterol levels and the HDL cholesterol to LDL cholesterol ratio had increased more in the Ca group than in the placebo group (mean between-group differences in change from baseline: for HDL cholesterol, 0.09 mmol/L (95% confidence interval [CI]: 0.02 to 0.17; P = 0.01); for HDL/LDL cholesterol ratio, 0.05 (95% CI: 0.02 to 0.08; P = 0.001)). This was largely due to a 7% increase in HDL cholesterol levels in the Ca group, with a nonsignificant 6% decline in LDL cholesterol levels. was no significant treatment effect on triglyceride level (P = 0.48). Calcium citrate supplementation causes beneficial changes in circulating lipids in postmenopausal women. suggests that a reappraisal of the indications for Ca supplementation is

necessary, and that its cost effectiveness may were underestimated. REFERENCE COUNT: THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS 31

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004070368 EMBASE

TITLE: Effects of Calcium Supplementation on Circulating

Lipids: Potential Pharmacoeconomic Implications.

AUTHOR: Reid I.R.

Prof. I.R. Reid, Department of Medicine, University of CORPORATE SOURCE:

Auckland, Private Bag 92019, Auckland, New Zealand.

i.reid@auckland.ac.nz

SOURCE: Drugs and Aging, (2004) Vol. 21, No. 1, pp. 7-17. .

Refs: 34

ISSN: 1170-229X CODEN: DRAGE6

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery

> 036 Health Policy, Economics and Management

037 Drug Literature Index 038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20040304

Last Updated on STN: 20040304

AR For about a century there has been recognition that calcium and lipids bind to one another in the gut, each interfering with the other's absorption. Calcium also causes malabsorption of bile acids, which is likely to contribute further to malabsorption of fat. dietary calcium intakes may also have stimulatory effects on

lipolysis. These mechanisms provide a basis for hypothesising that calcium supplementation may impact on circulating lipid concentrations, and there is now a significant amount of observational and trial data indicating that this is the case. The largest randomised controlled trial of calcium effects on lipids was carried out in 223 healthy postmenopausal women, and found that low density lipoprotein-cholesterol (LDL-C) decreased 6.3% and high density lipoprotein-cholesterol (HDL-C) increased by 7.3% at 1-year. The resultant 16.4% increase in HDL-C/LDL-C ratio would be predicted to reduce cardiovascular event rates by 20-30%, which is consistent with the available observational data. There are no trial data addressing this question and it is possible that other lipid-lowering agents, such as hydroxymethylglutaryl coenzyme A reductase inhibitors, might impact on cardiac event rates by mechanisms other than by lowering cholesterol levels. Therefore, caution is appropriate in incorporating these findings into clinical practice, but the balance of evidence suggests that calcium is a cost-effective adjunct to the dietary management of hyperlipidaemia.

## => d 1-11 L12 ibib abs

L12 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:411059 CAPLUS

DOCUMENT NUMBER: 142:469260

TITLE: HDL-boosting combination therapy complexes

INVENTOR(S): Tunac, Josefino B.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 15 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND DATE	APPLICATION NO.	DATE		
US 2005101561 WO 2005046662 WO 2005046662	A1 20050512 A2 20050526 A3 20050623	WO 2004-US37324	20041108 20041108		
W: AE, AG, A CN, CO, Cl GE, GH, GI LK, LR, L NO, NZ, OI TJ, TM, TI RW: BW, GH, GI AZ, BY, KO EE, ES, F	L, AM, AT, AU, AZ, R, CU, CZ, DE, DK, M, HR, HU, ID, IL, S, LT, LU, LV, MA, M, PG, PH, PL, PT, N, TR, TT, TZ, UA, M, KE, LS, MW, MZ, G, KZ, MD, RU, TJ, I, FR, GB, GR, HU, K, TR, BF, BJ, CF,	BA, BB, BG, BR, BW, BY, DM, DZ, EC, EE, EG, ES, IN, IS, JP, KE, KG, KP, MD, MG, MK, MN, MW, MX, RO, RU, SC, SD, SE, SG, UG, US, UZ, VC, VN, YU, NA, SD, SL, SZ, TZ, UG, TM, AT, BE, BG, CH, CY, IE, IS, IT, LU, MC, NL, CG, CI, CM, GA, GN, GQ,	FI, GB, GD, KR, KZ, LC, MZ, NA, NI, SK, SL, SY, ZA, ZM, ZW ZM, ZW, AM, CZ, DE, DK, PL, PT, RO,		

PRIORITY APPLN. INFO.:

US 2003-518091P P 20031107

AB A pharmaceutical composition including therapeutically effective amts. of at least one HMG-CoA reductase inhibitor present as a dyhydroxyacid salt and at least one addnl. therapeutic agent is claimed. Dehydroxy acid salt of sodium lovastatin (I) was prepared and its antilipidemic activity was studied in hamster. A repeat side-by-side comparison between I and Lipitor at 5-20 mg dose range confirmed the effectiveness of I in decreasing LDL, moreover, I was effective at a dose as low as 5 mg.

L12 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:878382 CAPLUS

DOCUMENT NUMBER: 141:350161

TITLE: Preparation of azole compounds as PTP1B inhibitors

Ikemoto, Tomoyuki; Tanaka, Masahiro; Yuno, Takeo; Sakamoto, Johei; Nakanishi, Hiroyuki; Nakagawa, INVENTOR(S):

Yuichi; Ohta, Takeshi; Sakata, Shohei; Morinaga,

Hisayo

Japan Tobacco Inc., Japan PCT Int. Appl., 542 pp. PATENT ASSIGNEE(S):

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

FAMILY ACC. NUM. COUNT:

Japanese

PATENT INFORMATION:

PA	PATENT NO.			KIND DATE		APPLICATION NO.				DATE								
WO	2004	0899	18		A1		2004	1021	,	WO 2	004-	JP51:	19		2	0040	409	
	W:	ΑE,	AG,	AL,	ΑM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,	
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FΙ,	GB,	GD,	
		GE,	GH,	GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	ΝA,	NI,	
		NO,	ΝZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	
								UA,										
	RW:							ΜZ,										
		BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	ΑT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	
		ES,	FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,	SI,	
		-	-	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	
		TD,								-								
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EP	1553							0713										
	R:							FR,										
								MK,										HR
JP	2005	2724	76		A2		2005	1006		JP 2	005-	1337	55		20	0050	428	
PRIORIT	RIORITY APPLN. INFO.:										1052							
												1575			A 20	0030	603	
												5053			A3 20			
									1	WO 2	004-	JP51:	19	Ī	v 20	0040	409	
OTHER SOURCE(S):				MAR	PAT	141:	3501	61										

$$R - \left[L\right] - \left[CH_{2}\right] - X - \left[C\right] - \left[CH_{2}\right] - \left[CH_$$

AB Title compds. I [V = N, CH; W = S, O; m = 0-2; R1, R2 = H, alkyl; X = NR4, etc.; R4 = H, alkyl; n = 0-4; p = 0, 1; L = CR20R21, etc.; R20 = H, alkyl, etc.; R21 = H, alkyl, etc.; R = CO2R19, etc.; R19 = H, alkyl; B = aryl, heteroaryl; R3 = H, halo, etc.; Y = 0, etc.; s = 0, 1; A = (un)substituted alkylene with cycloalkyl; Z = cycloalkyl, etc.] were prepared For example, O-alkylation of 5-hydroxynicotinic acid Me ester with compound II [Q = Cl], e.g., prepared from 4-bromoacetylbenzoic acid in 5 steps, followed by saponification

afforded compound II [3-carboxypyridin-5-yloxy] in 44.1% overall yield. In PTP1B (protein tyrosine phosphatase 1B) inhibition assays, the IC50 value of compound II [Q = 3-carboxypyridin-5-yloxy] was 0.28  $\mu$ M. Compds. I are claimed useful for the treatment of obesity, diabetes, etc. Formulations are given.

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004070368 EMBASE

TITLE: Effects of Calcium Supplementation on Circulating

Lipids: Potential Pharmacoeconomic Implications.

AUTHOR: Reid I.R.

CORPORATE SOURCE: Prof. I.R. Reid, Department of Medicine, University of

Auckland, Private Bag 92019, Auckland, New Zealand.

i.reid@auckland.ac.nz

SOURCE: Drugs and Aging, (2004) Vol. 21, No. 1, pp. 7-17. .

Refs: 34

ISSN: 1170-229X CODEN: DRAGE6

COUNTRY: New Zealand

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 018 Cardiovascular Diseases and Cardiovascular Surgery

036 Health Policy, Economics and Management

037 Drug Literature Index 038 Adverse Reactions Titles

048 Gastroenterology

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20040304

Last Updated on STN: 20040304

For about a century there has been recognition that calcium and AB lipids bind to one another in the gut, each interfering with the other's absorption. Calcium also causes malabsorption of bile acids, which is likely to contribute further to malabsorption of fat. High dietary calcium intakes may also have stimulatory effects on lipolysis. These mechanisms provide a basis for hypothesising that calcium supplementation may impact on circulating lipid concentrations, and there is now a significant amount of observational and trial data indicating that this is the case. The largest randomised controlled trial of calcium effects on lipids was carried out in 223 healthy postmenopausal women, and found that low density lipoprotein-cholesterol (LDL-C) decreased 6.3% and high density lipoprotein-cholesterol (HDL-C) increased by 7.3% at 1-year. The resultant 16.4% increase in HDL-C/LDL-C ratio would be predicted to reduce cardiovascular event rates by 20-30%, which is consistent with the available observational data. There are no trial data addressing this question and it is possible that other lipid-lowering agents, such as hydroxymethylglutaryl coenzyme A reductase inhibitors, might impact on cardiac event rates by mechanisms other than by lowering cholesterol levels. Therefore, caution is appropriate in incorporating these findings into clinical practice, but the balance of evidence suggests that calcium is a cost-effective adjunct to the dietary management of hyperlipidaemia.

L12 ANSWER 4 OF 11 MEDLINE on STN 2002342613 ACCESSION NUMBER: MEDLINE PubMed ID: 12085783

DOCUMENT NUMBER:

TITLE:

Calcium's healthy cholesterol consequences.

AUTHOR: Anonymous

Health news (Waltham, Mass.), (2002 Jun) Vol. 8, No. 6, pp. SOURCE:

Journal code: 9800495. ISSN: 1081-5880.

United States PUB. COUNTRY: News Announcement DOCUMENT TYPE:

LANGUAGE: English

FILE SEGMENT: Consumer Health

200206 ENTRY MONTH:

ENTRY DATE: Entered STN: 20020628

> Last Updated on STN: 20020628 Entered Medline: 20020627

L12 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:696671 CAPLUS

DOCUMENT NUMBER: 137:216323

TITLE: Method of administering calcium

citrate

INVENTOR(S): Reid, Ian R.

PATENT ASSIGNEE(S): Uniservices Ltd., N. Z.

U.S. Pat. Appl. Publ., 13 pp. SOURCE:

CODEN: USXXCO

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.			KIND DATE				APPLICATION NO.					DATE				
	US 2002128320						US 2001-16371					20011210					
									WO 2002-IB5759					20021210			
	WO 200																
	W:	AE,															
							DK,										
		•	•	•	•		IN,		•	•		•	•			•	•
		•		•			MD,				•		•		•		•
				-	-		SD,					ТJ,	TM,	TN,	TR,	TT,	TZ,
		•	•	•	,		VN,	•									
	RW	: GH,	-		-	-			-	-	-		•		-	-	•
		•	•		-		TM,		-	-	-		•				•
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L12 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN
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ACCESSION NUMBER: 2002:392237 CAPLUS

DOCUMENT NUMBER: 136:401651

TITLE: Preparation of fused pyridine derivatives as HMG-CoA

reductase inhibitors

Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing INVENTOR(S):

PATENT ASSIGNEE(S):

SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.

CODEN: USXXCO

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	US 2002061901	A1	20020523	US 2001-8154	20011204
	US 6620821	В2	20030916		
	US 2002028826	A1	20020307	US 2001-875218	20010606
	US 2004024216	A1	20040205	US 2003-602753	20030624
PRIOR	RITY APPLN. INFO.:	•		US 2000-211594P	20000615
				US 2001-875218 A	12 20010606
				US 2001-8154 A	3 20011204
001100	0011000 (0)	143 D D 7 M	100 401001		

OTHER SOURCE(S):

MARPAT 136:401651

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$$R^2$$
 $R^2$ 
 $N = (O)_n$ 
 $CO_2Na$ 
 $R^4$ 
 $R^4$ 
 $R^4$ 

AΒ The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl; R4 = H, halo, CF3, OH, alkyl, alkoxy, CO2H, (un)substituted NH2, cyano, (un) substituted CONH2, etc.; R7 = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Prepns. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

L12 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1 ACCESSION NUMBER: 2002:211581 CAPLUS

DOCUMENT NUMBER:

136:385392

TITLE: Effects of **calcium** supplementation on serum lipid concentrations in normal older women: A

randomized controlled trial

AUTHOR(S): Reid, Ian R.; Mason, Barbara; Horne, Anne; Ames, Ruth;

Clearwater, Judith; Bava, Usha; Orr-Walker, Brandon;

Wu, Fiona; Evans, Margaret C.; Gamble, Gregory D.

CORPORATE SOURCE: Department of Medicine, University of Auckland,

Auckland, N. Z.

SOURCE: American Journal of Medicine (2002), 112(5), 343-347

CODEN: AJMEAZ; ISSN: 0002-9343

PUBLISHER: Excerpta Medica, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

To determine the effect of supplementation with Ca citrate on circulating lipid concns. in normal older women. As part of a study of the effects of Ca supplementation on fractures, the authors randomly assigned 223 postmenopausal women (mean [ $\pm$  SD] age, 72  $\pm$  4 yr), who were not receiving therapy for hyperlipidemia or osteoporosis, to receive Ca (1 g/d, n = 111) or placebo (n = 112) for 1 yr. Fasting serum lipid concns., including high-d. lipoprotein (HDL) cholesterol and low-d. lipoprotein (LDL) cholesterol, were obtained at baseline, and at 2, 6, and 12 mo. After 12 mo, HDL cholesterol levels and the HDL cholesterol to LDL cholesterol ratio had increased more in the Ca group than in the placebo group (mean between-group differences in change from baseline: for HDL cholesterol, 0.09 mmol/L (95% confidence interval [CI]: 0.02 to 0.17; P = 0.01); for HDL/LDL cholesterol ratio, 0.05 (95% CI: 0.02 to 0.08; P = 0.001)). This was largely due to a 7% increase in HDL cholesterol levels in the Ca group, with a nonsignificant 6% decline in LDL cholesterol levels. was no significant treatment effect on triglyceride level (P = 0.48). Calcium citrate supplementation causes beneficial

changes in circulating lipids in postmenopausal women. This suggests that a reappraisal of the indications for Ca supplementation is necessary, and that its cost effectiveness may were underestimated.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2001:747110 CAPLUS

DOCUMENT NUMBER: 135:256481

TITLE: Manufacture of a cultured dairy product containing

exogenously added protein

INVENTOR(S): Nadland, Karl Johan
PATENT ASSIGNEE(S): Nutri Pharma Asa, Norway
SOURCE: Eur. Pat. Appl., 22 pp.

CODEN: EPXXDW

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1142482	A1	20011010	EP 2000-610033	20000404
R: AT, BE,	CH, DE, DK	, ES, FR,	GB, GR, IT, LI, LU, 1	NL, SE, MC, PT,
IE, SI,	LT, LV, FI	, RO		
WO 2001074171	A1	20011011	WO 2001-IB553	20010403
W: AE, AG,	AL, AM, AT	, AT, AU,	AZ, BA, BB, BG, BR, I	BY, BZ, CA, CH,
CN, CO,	CR, CU, CZ	, CZ, DE,	DE, DK, DK, DM, DZ, 1	EE, EE, ES, FI,
FI, GB,	GD, GE, GH	, GM, HR,	HU, ID, IL, IN, IS,	JP, KE, KG, KP,
KR, KZ,	LC, LK, LR	, LS, LT,	LU, LV, MA, MD, MG, I	MK, MN, MW, MX,
MZ, NO,	NZ, PL, PT	, RO, RU,	SD, SE, SG, SI, SK, S	SK, SL, TJ, TM,
TR, TT,	TZ, UA, UG	, US, UZ,	VN, YU, ZA, ZW, AM, Z	AZ, BY, KG, KZ,
MD, RU,	TJ, TM			

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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2001046748
                           Α5
                                  20011015
                                               AU 2001-46748
                                                                        20010403
     US 2002012719
                                               US 2001-828486
                                  20020131
                                                                        20010409
                            A1
PRIORITY APPLN. INFO.:
                                               EP 2000-610033
                                                                     A 20000404
                                               US 2000-195988P
                                                                     Ρ
                                                                        20000407
                                               WO 2001-IB553
                                                                     W
                                                                        20010403
AB
     Cultured dairy products are formulated to contain exogenously added
     protein and optionally exogenously added dietary fiber. The methods
     comprise the steps of (i) hydrating a protein source by subjecting it to
     shear forces and if necessary to heat in the presence of excess of water;
     (ii) adding the hydrated protein source from step (i) to a milk composition;
     (iii) adding a fermentation culture to the mixture from step (ii); and (iv)
     fermenting to obtain a cultured dairy product. The shear forces are
     preferably applied by use of a homogenizer at a temperature of 80°. The
     exogenously added proteins are preferably soy proteins and the exogenously
     added dietary fibers are preferably soybean fiber, especially soybean cotyledon
     fibers. The cultured dairy products preferably contain exogenously added protein in an amount of \geq 5\% by weight Thus, a suitable protein source
     may include soy protein 10.66, soybean cotyledon fiber 2.67, and soy
     lecithin 0.76% (weight percent of cultured dairy product).
REFERENCE COUNT:
                                 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
                                 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 9 OF 11 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights
L12
     reserved on STN
ACCESSION NUMBER:
                     2000398596 EMBASE
                     Heparin-free DALI LDL-apheresis in hyperlipidemic patients:
TITLE:
                     Efficacy, safety and biocompatibility.
AUTHOR:
                     Wendler T.; Lennertz A.; Heinemann O.; Duhr C.; Samtleben
                     W.; Bosch T.
                     Dr. T. Bosch, Schwerpunkt Nephrologie, Medizinische Klinik
CORPORATE SOURCE:
                     I, Klin. Grosshadern der Univ. Munchen, D-81366 Munchen,
                     Germany. bosch@med1.uni-muenchen.de
SOURCE:
                     International Journal of Artificial Organs, (2000) Vol. 23,
                     No. 10, pp. 710-717. .
                     Refs: 19
                     ISSN: 0391-3988 CODEN: IJAODS
COUNTRY:
                     Italy
DOCUMENT TYPE:
                     Journal; Article
                              Cardiovascular Diseases and Cardiovascular Surgery
FILE SEGMENT:
                     018
                              Internal Medicine
                     006
                     030
                              Pharmacology
                     025
                              Hematology
                     029
                              Clinical Biochemistry
                     038
                              Adverse Reactions Titles
                     037
                              Drug Literature Index
                     003
                              Endocrinology
LANGUAGE:
                     English
SUMMARY LANGUAGE:
                     English
ENTRY DATE:
                     Entered STN: 20001213
                     Last Updated on STN: 20001213
AB
     Background and aim of the study. In routine DALI apheresis - the first
     technique for direct adsorption of lipoproteins from whole blood - heparin
     plus citrate (ACD-A) is used as anticoagulation regimen.
     However, recently several publications have warned of heparin-induced
     thrombocytopenia as a rare but potentially life-threatening complication
     of heparin administration (HIT type 2). The aim of the present study was
     therefore to test the efficacy and biocompatibility of DALI using a
     heparin-free anticoagulation regimen consisting exclusively of
     citrate. Methods. Four symptomatic hypercholesterolemic patients
     on regular DALI apheresis were switched to the heparin-free protocol for
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two sessions each. Two of the patients were on oral anticoagulation using

phenprocoumon. In the weekly sessions, 1.3 patient blood volumes were processed at a blood flow rate of 60 ml/min using ACD-A at a ratio of 1:20 (v/v) during adsorber priming and the session. Results. Clinically, all sessions were essentially uneventful. Uncorrected liporpotein reductions amounted to 65% for LDL-C, 62% for Lp(a), 53% for VLDL-C, 24% for HDL-C, 17% for triglycerides and 19% for fibrinogen. Cell counts remained virtually constant. No signs of hemolysis or clotting could be detected. Thromboplastin time (Quick) was slightly prolonged and partial thromboplastin time (PTT) moderately elevated in all patients. In contrast, whole blood coagulation time acc. to Lee-White and activated clotting times were increased only in orally anticoagulated patients. Biocompatibility in terms of complement, leukocyte and thrombocyte activation was excellent. Bradykinin activation was moderate peaking at 3038 pg/ml in the efferent line. Systemic thrombin-antithrombin complex (TAT) reflected perfect anticoagulation in orally anticoagualted patients and adequate anticoagulation in the patients without phenprocoumon. Conclusion. In this pilot study heparin-free DALI apheresis was safe and effective and may thus be performed in LDL-apheresis dependent patients who suffer from heparin intolerance.

L12 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 1993:471434 CAPLUS

DOCUMENT NUMBER: 119:71434

TITLE: Short-term dietary calcium fortification

increases fecal saturated fat content and reduces

serum lipids in men

AUTHOR(S): Denke, Margo A.; Fox, Mary M.; Schulte, Marcia C.

CORPORATE SOURCE: Southwest. Med. Cent., Univ. Texas, Dallas, TX,

75235-9052, USA

SOURCE: Journal of Nutrition (1993), 123(6), 1047-53

CODEN: JONUAI; ISSN: 0022-3166

DOCUMENT TYPE: Journal LANGUAGE: English

The effect of dietary Ca on fecal fatty acid excretion and serum lipids was tested in a randomized, single-blind metabolic study in 13 healthy men with moderate hypercholesterolemia. A low-Ca base diet containing 34% of energy from fat, 13% from saturated fatty acids, 240 mg cholesterol/day, and 410 mg Ca/day was compared with a fortified version in which Ca citrate malate was added to orange juice (550 mg), muffins (750 mg), and 2 tablets (500 mg) for a total Ca intake of 2200 mg/day. Fecal collections (72 h, days 8, 9, 10) and blood from fasting subjects for lipids and lipoproteins (days 9, 10, 11) were obtained. The percentage of dietary saturated fat excreted per day increased from 6 to 13% with Ca fortification. There was no change in fecal bile acid excretion. The high-Ca diet significantly reduced total cholesterol by 6% (5.99 to 5.66 mmol/L), LDL cholesterol by 11% (4.13 to 3.67 mmol/L), and apolipoprotein B concns. by 7% when compared with the low-Ca diet. There was no change in HDL cholesterol or apolipoprotein Al concns. Urinary Ca excretion increased from 146 to 230 mg/day when the high-Ca diet was consumed. Ca fortification was effective in lowering total and LDL cholesterol-lowering diet therapy.

L12 ANSWER 11 OF 11 MEDLINE on STN ACCESSION NUMBER: 87049045 MEDLINE DOCUMENT NUMBER: PubMed ID: 3778574

TITLE: Atherogenesis. Mitigation of monocyte adhesion to arterial

endothelium in hyperlipidemic rats by phosphocitrate, a

phosphorylated polycarboxylic acid.

AUTHOR: Shankar R; Tuyethong N; Sallis J D

SOURCE: Atherosclerosis, (1986 Oct) Vol. 62, No. 1, pp. 47-54.

Journal code: 0242543. ISSN: 0021-9150.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198612

ENTRY DATE: Entered STN: 19900302

Last Updated on STN: 19900302 Entered Medline: 19861215

AB Phosphocitrate, a phosphorylated polycarboxylic acid ameliorates two early events in atherogenesis. When administered to rats on an atherosclerotic diet (112 mumol/kg body weight/day), it reduced monocyte adhesion to aortic endothelium from 34 +/- 7 cells/HPF for untreated rats to 1 +/- 1 cell/HPF, a value seen in normal, non-atherosclerotic rats. Transmission electron microscopy of aortic sections showed no evidence of subendothelial lipid accumulation in phosphocitrate-treated rats despite the high circulating plasma lipid levels. The mechanisms of action of phosphocitrate are unknown but the indications are that its influence may be mediated through its polyanionic chemical nature and/or its ability to modulate cellular calcium accumulation. In addition to its possible therapeutic value as an anti-calcifying and anti-atherogenic compound, phosphocitrate may prove useful as an experimental probe for studying the cellular basis of atherogenesis.

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